Exhibit 1

Expert Report of Professor David Cutler

March 25, 2019

national and international organizations devoted to the study of health economics, such as the American Society of Health Economists (ASHEcon) and the International Health Economics Association (IHEA).[9] There are also numerous conferences devoted to health economics, several journals in the field (e.g. Journal of Health Economics, Health Affairs), textbooks on the topics, and courses on health economics taught at a large number of universities in the US and abroad.

14. Within the field of health economics, a major focus of study has been understanding markets for products with health risks. This includes analysis of tobacco use, alcohol intake, excessive food consumption, and, more recently, excessive use of opioids. In analyzing these topics, scholars have evaluated and published research on issues such as what actions on the part of corporations lead to excessive use of these substances and how excessive use of substances affects public budgets. The field also has extensive experience understanding how use of substances is related to personal harms such as mortality and morbidity. Specific studies on the harms of opioids are referred to later in this report. These studies, which build off decades of work by health economists, are authored by academics, private researchers and government agencies and are widely used in setting policy.

15. The remainder of this report is organized as follows:

- Section III presents an overview of the framework used to calculate the percentage of harms incurred by the Bellwether divisions that is attributable to prescription opioid shipments.
- Section IV presents estimates of the share of various harms faced by Bellwether jurisdictions that is due to opioids.

[9] https://www.ashecon.org/; https://www.healtheconomics.org/.

- Section V presents alternative approaches to estimating the impact of shipments of prescription opioids on mortality.
- Section VI summarizes estimates of mortality that can be attributed to defendants' misconduct, which incorporate estimates from the Rosenthal Report on the effect of defendants' misconduct on prescription opioid shipments.
- Section VII presents estimates of the share of various opioid-related harms faced by Bellwethers that are attributable to defendants' misconduct.
- Section VIII presents a supplemental analysis of the impact of opioids on crime.

III. Framework for Evaluating the Effect of Prescription Opioid Shipments on Harms that Imposed Costs on Bellwether Governments

16. As the review of the opioid crisis in the Gruber Report shows, it is widely recognized that the opioid crisis has resulted in a variety of social harms including increased mortality from both prescription and illicit opioids, increased trafficking in heroin and other illicit opioids, and increased demand for police services, criminal justice services, addiction treatment services, services for children and families, and first responder services, among other harms.

17. Analysis of the link between opioid shipments and harms is complicated by features of the opioid marketplace which make it unique among pharmaceuticals.[10] First, there is a substantial set of illegal opioids which are closely related chemically to legal opioids. For example, heroin and synthetic fentanyl are close chemical analogues to the active substances in legal opioids.[11] Available evidence indicates that licit and illicit opioids are to some degree substitutes. The analysis thus needs to explicitly consider harms due to any use of illicit opioids that resulted from defendants' actions along with harms due to licit opioids. The analysis also

[10] See Gruber Report for additional discussion.

[11] See, for example, Kosten, Thomas R., and Tony P. George. "The neurobiology of opioid dependence: implications for treatment." *Science & Practice Perspectives* 13 (2002): 13-20. I understand this is also addressed in the Expert Report of Dr. Katherine Keyes.

needs to account for the consequences of public and private policy interventions that decreased the availability of some licit opioid products which, in turn, led people to turn to illicit, more harmful, opioids. Each of these factors influences the nature of the empirical analysis.

18. The approach that is used here for estimating harms is depicted in **Figure III.1** below. defendants' misconduct is shown in the blue boxes in the upper part of the figure. This conduct includes, but is not limited to, the misrepresentations of the risks and benefits of opioid therapy by manufacturer defendants and the failure to detect and prevent excessive opioid shipments by all registrants of the Controlled Substances Act ("CSA"), including the distributor defendants. For the purposes of my analysis, I assume defendants' misconduct directly influences sales and shipments of prescription opioids, as presented in the Rosenthal Report. Excessive use of prescription opioids, in turn, leads to the variety of harms noted above: law enforcement, courts, child-related, and public health problems. The policy response to these problems played out on a number of levels, including: federal, state, and local policy; policy changes by private and public insurers; recommendations and restrictions implemented by medical societies and health care organizations; and changes by pharmaceutical companies. Together, these various policies contributed to increased use of illicit opioids and further harms, none of which would have been expected to occur in the absence of defendants' actions.

48. Due to changes over time in how prescription opioid shipments affect mortality, and due to limitations of available data, two different statistical regression frameworks are applied to estimate the impact of shipments of prescription opioids on mortality. As noted above, the "direct approach" is based on the relationship between changes over time in opioid mortality across different geographic areas and shipments of prescription opioids to those areas. The "indirect approach" uses the relationship between opioid mortality across areas and social and economic characteristics of those areas prior to defendants' misconduct to project changes in opioid-related mortality expected in the absence of excessive shipments of prescription opioids (i.e. the level of prescription opioid shipments in excess of those that would be expected given the observed changes in the social and economic characteristics). The choice and application of both approaches is informed by the changing nature of the opioid crisis.

49. This section first describes the changing nature of the opioid crisis and how that guides the choice of the statistical modelling approaches. Afterwards, the implementation of these statistical models is discussed.

A. The Shift in the Relationship Between Prescription Opioid Shipments and Opioid Mortality Over Time

50. As discussed in the Gruber Report, there are distinct phases of the current opioid epidemic, with 2010 marking an approximate transition point for the beginning of the decline in overall prescription opioid shipments. Before this transition, the crisis was characterized by large and on-going increases in the shipments of prescription opioids and rapid increases in mortality associated with prescription opioids. For example, between 1999 and 2010, 85

percent of the increase in opioid mortality was attributable to increases in prescription opioid mortality.

51. In addition to the immediate damage it caused, the increase in opioid shipments prior to 2010 created a large number of opioid addicts. As noted in the Gruber Report, the existence of widespread dependence on opioids, coupled with a decline in the available supply of prescription opioids after 2010, led to an increased demand for illicit opioids, first heroin and later fentanyl.

52. Between 2010 and 2016, prescription (i.e. licit) opioid shipments fell. There were many causes of this including but not limited to: OxyContin was reformulated in an attempt to make it more difficult to abuse;[34] medical organizations began warning against excessive prescribing of opioids; and federal and state governments began expanding enforcement against "pill mills" and other forms of diversion of prescription opioids for non-medical use.[35] The FDA pointed to these various factors in their review of whether Purdue's reformulated OxyContin reduced abuse of the drug.[36]

53. While identification of the precise role of any individual supply-reducing factor is beyond the scope of this report, the development of abuse-deterrent formulations as well as other supply-limiting interventions clearly failed to eliminate either the widespread pre-existing

[34] As the FDA has argued, reformulation did not eliminate the potential for OxyContin to be abused as it is still possible to be abused orally (PPLPC005000211723, at 383).
[35] See, for example: National Academies of Science, "Pain Management and the Opioid Epidemic: Balancing Societal and Individual Benefits and Risks of Prescription Opioid Use," National Academies Press (2017), at p. 29 and 36; Evans, William N., Ethan Lieber, Patrick Power. "How the Reformulation of Oxycontin Ignited the Heroin Epidemic." Review of Economics and Statistics 101 no. 1 (2019): 1-15 (Evans et al. (2019)), at p. 11.
[36] PPLPC005000211723, at 28

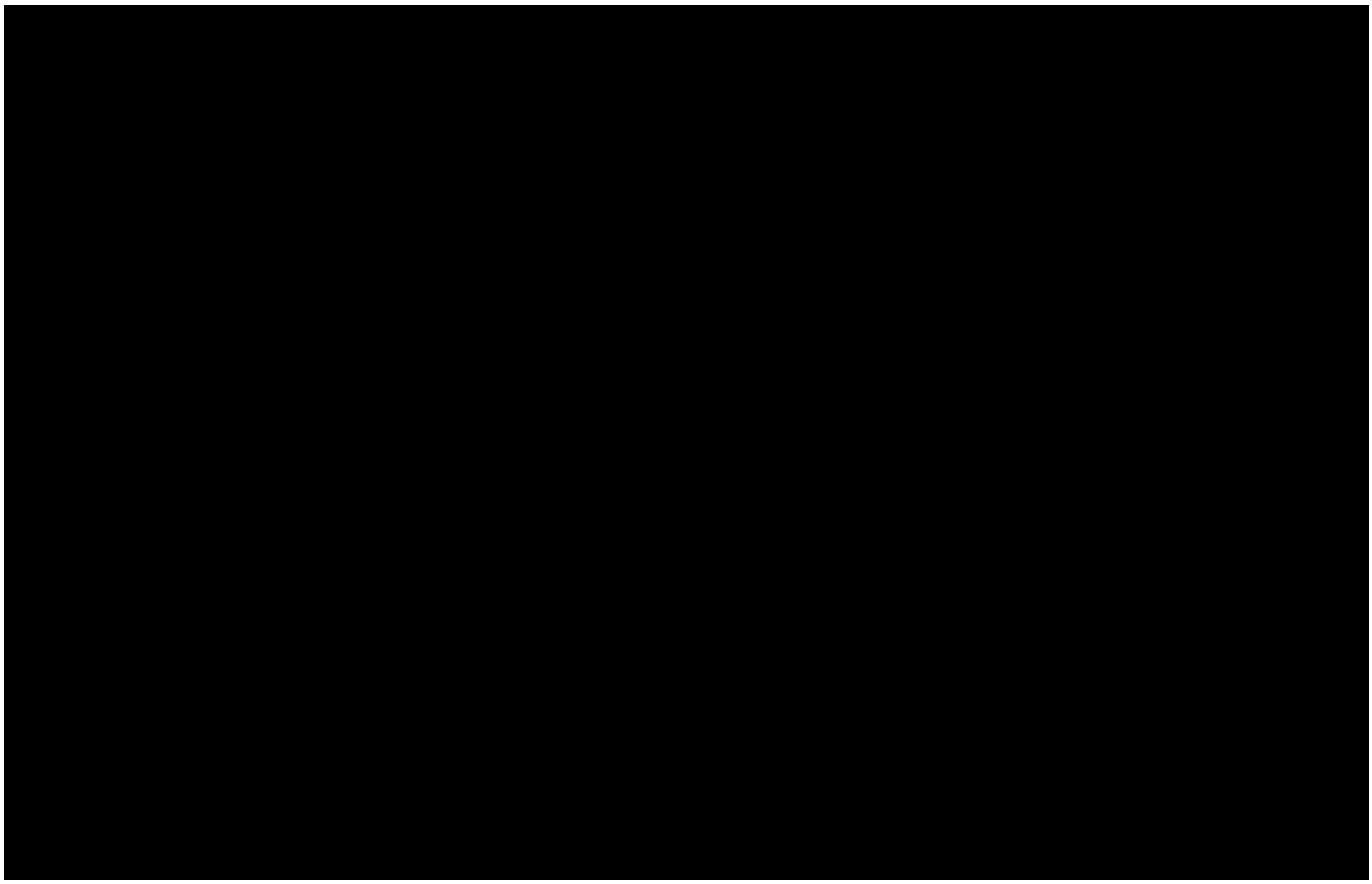
dependence on opioids, or the addiction risk and the potential for abuse of illicit opioids. Furthermore, as also concluded by Professor Gruber, the increase in the demand for illicit opioids, and the associated increases in mortality, would not have occurred in the absence of the enormous increase in prescription opioid shipments resulting from defendants' misconduct, which effectively created a stock of individuals susceptible to illicit opioid use and abuse.

54. The combined consequence of these factors was a rapid growth in misuse of illicit opioids and increase in mortality due to heroin and fentanyl which began around 2010. The increase in deaths due to illicit opioid use far exceeded the decline in mortality associated with prescription opioids and thus, as a result, total mortality rose even as legal opioid shipments fell.

55. In short, the nature of the opioid crisis changed around 2010. This resulted in a shift in the relationship between shipments of prescription opioids and mortality that has been widely recognized in the economic literature.[37] Here, the shift reflects the dramatic increase in heroin-related mortality post-2010, which is confirmed by statistical analysis of changes in trends in heroin-related overdose mortality from 1999-2014. (The analysis is limited to this period given that the emergence of fentanyl resulted in further acceleration in deaths due to illicit opioid use around 2014).

56. To capture this shift in the relationship between shipments and mortality, a statistical analysis identified the month that best identifies the date at which the time series of heroin

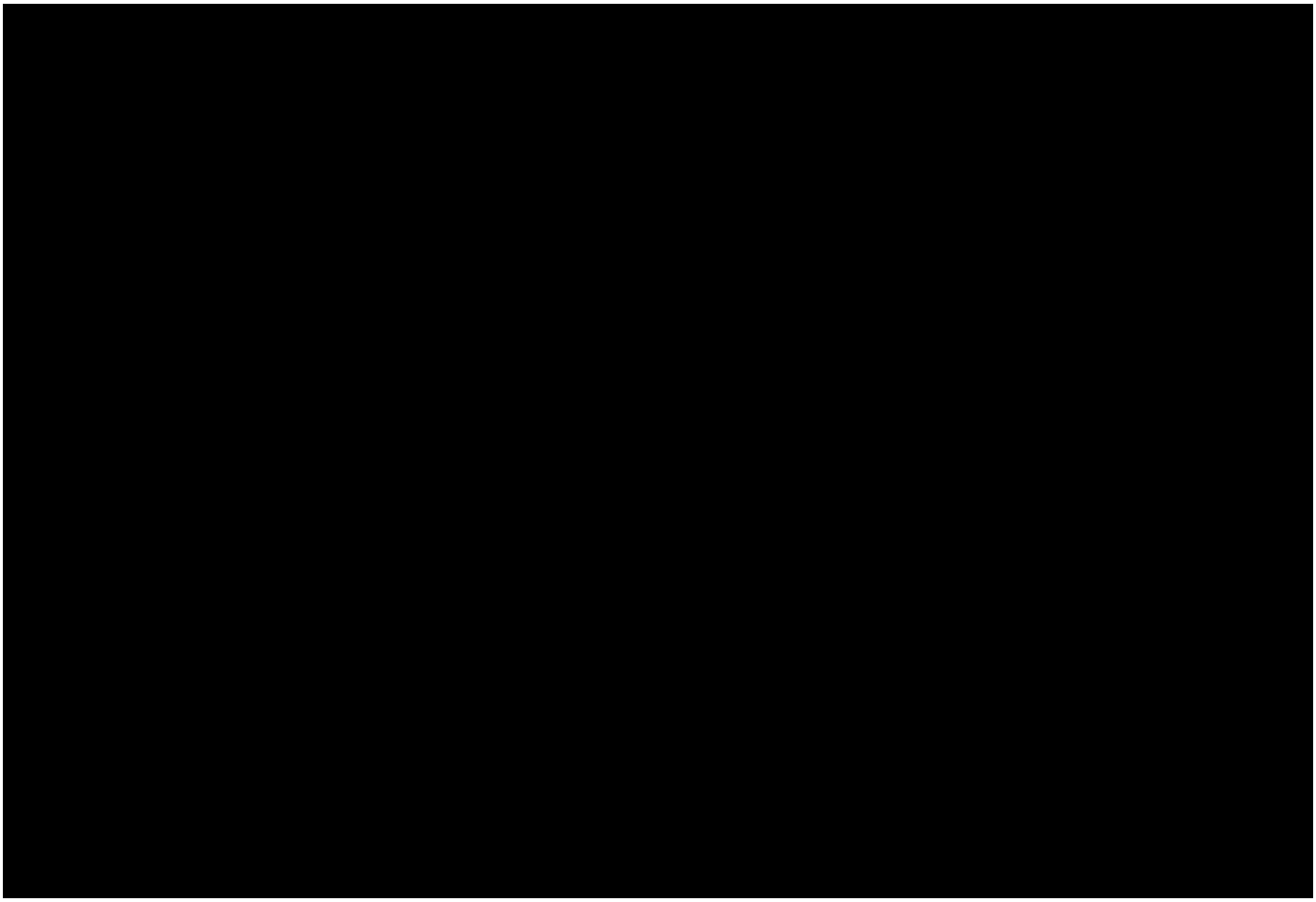
[37] For example, *see*: Evans, et al (2019); Alpert, Abby, David Powell, and Rosalie Liccardo Pacula. "Supply-Side Drug Policy In The Presence Of Substitutes: Evidence From The Introduction Of Abuse-Deterrent Opioids." *American Economic Journal: Economic Policy* 10 (2018): 1-35.



[38] See Chow, Gregory C. "Tests of equality between sets of coefficients in two linear regressions." *Econometrica: Journal of the Econometric Society* 28 (1960): 591-605; Quandt, Richard E. "Tests of the hypothesis that a linear regression system obeys two separate regimes." *Journal of the American statistical Association* 55 (1960): 324-330; Fisher, Franklin M. "Tests of equality between sets of coefficients in two linear regressions: An expository note." *Econometrica: Journal of the Econometric Society* 28 (1970): 361-366; An F-statistic is used in econometrics to test whether the values across two groups differ from each other. The largest F-statistic identifies the month associated with the largest difference in the trends (growth rates) of heroin mortality between the two periods.
[39] Evans et al. (2019) present a similar analysis and reach a similar conclusion.

Source: NCHS Mortality Data

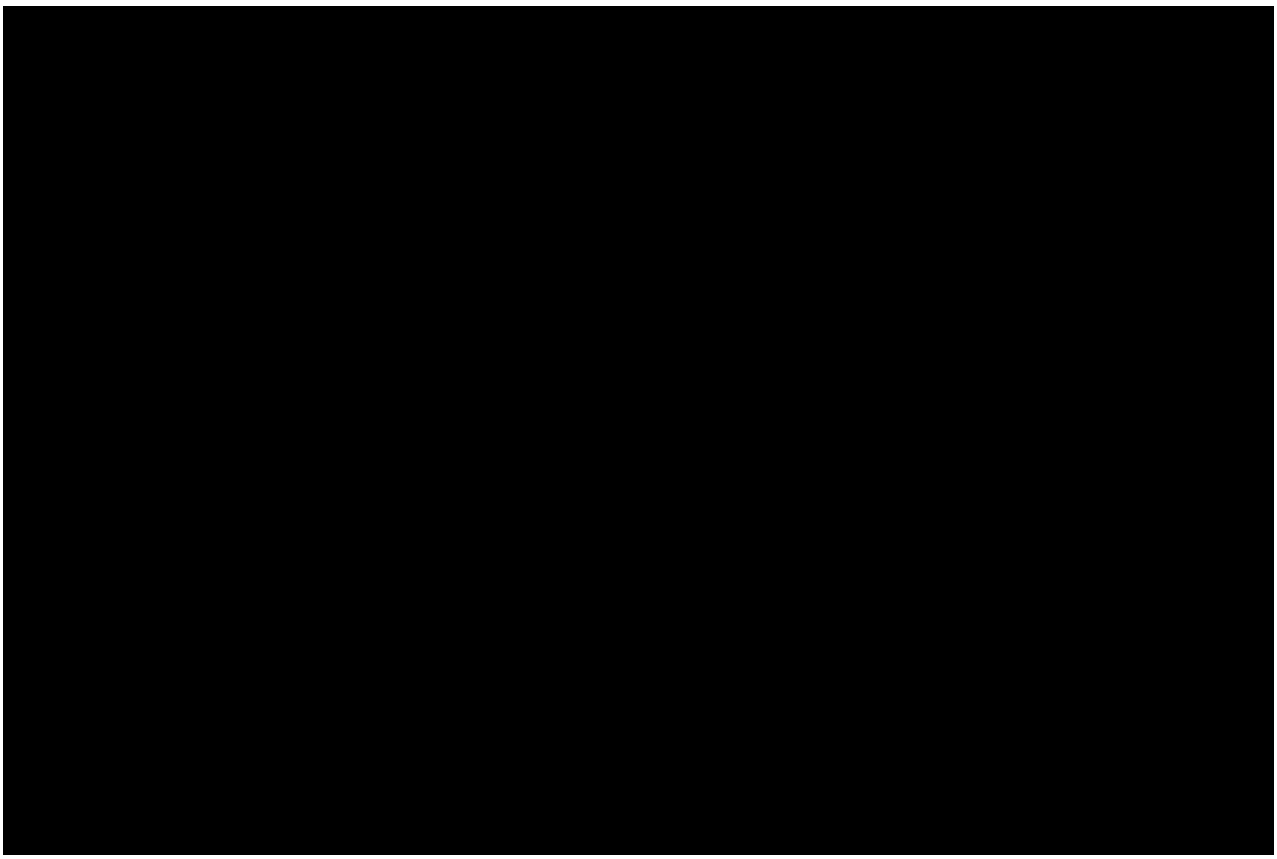
58. Consistent with the events described above, mortality associated with prescription opioids (not involving illicit opioids) also started to decline around the same time as the acceleration of illicit opioid deaths. A similar analysis establishes that the long-term trend of increasing prescription opioid mortality was reversed around the same time and that the best estimate of this shift was December 2010. **Figure III.3** reports the prescription opioid mortality rates and the regression estimate of the trends before and after the best estimate of the date of the shift in the rate.



Source: NCHS Mortality Data

59. The shift in the nature of the opioid crisis does not mean that historical levels of shipments are irrelevant to understanding the emergence of heroin opioid mortality. To the contrary, available data demonstrate that the increase in heroin-related mortality was greatest in counties with high historical levels of shipments and lower in areas with relatively lower levels of historical shipments. This pattern is consistent with the view that (i) historical shipments (and the consequent opioid dependence) played an important role in contributing to the demand for illicit opioids after 2010, and (ii) factors such as reduced shipments of prescription opioids and development of abuse deterrent formulations resulted in an increased demand for illicit opioids in all areas.

60. These effects are clearly demonstrated in the results of performing an additional test on annual heroin mortality data from two groups of counties: those with shipments of prescription opioids from 1997-2010 within the top 25% of counties ("high shipment counties") and those with shipments in the bottom 25% of counties ("low shipment counties").[40] **Figure III.4** summarizes this test, which establishes that while both areas have clear shifts in the trend in heroin mortality after 2010, the acceleration in heroin mortality is significantly larger in the high shipment counties. The difference in the change in slope and level is statistically significant.



Source: NCHS Mortality Data and ARCOS

[40] County-specific mortality data are only available on an annual basis. National data are available on a monthly basis.

61. This finding is consistent with the economic literature that has studied the transition from prescription to illicit opioids in the post-2010 time period. For example, Evans et al. (2019) evaluated a similar set of statistical tests using state-level mortality data and found evidence of substitution from prescription opioids to heroin. They conclude that "there appears to have been one-for-one substitution of heroin deaths for opioid deaths."[41] Similarly, Alpert et al. 2018 analyzed prescription shipments and mortality data in a panel data context and concluded that areas with high levels of abuse of OxyContin are associated with large increases in heroin mortality following 2010.[42] The same authors have now extended the work to study the growth in infections of hepatitis C since 2010 and conclude that areas with higher levels of OxyContin abuse have seen much larger growth in the virus, which is frequently contracted through intravenous drug use.[43]

62. Moreover, a number of epidemiological studies have established that much of the increase in the use of illicit opioids after 2010 was the result of addictions resulting from prior use of prescription opioids. Several of the studies are reviewed in the Gruber Report, so they are only briefly noted here.[44] Key studies establish that:

- A survey of heroin patients in drug treatment centers that reported initiating use in the 2000s established that 75 percent initiated opioid use with prescription opioids.

[41] Evans et al. (2019), at p. 2.
[42] Alpert, Abby, David Powell and Rosalie Liccardo Pacula. "Supply-Side Drug Policy in the Presence of Substitutes: Evidence from the Introduction of Abuse-Deterrent Opioids." *American Economic Journal: Economic Policy* 10 (2018): 1-35, p. 4.
[43] Powell, David, Abby Alpert, and Rosalie L. Pacula. "A Transitioning Epidemic: How the Opioid Crisis is Driving the Rise in Hepatitis C." *Health Affairs* 38 no. 2 (2019): 287-294.
[44] I understand that the Expert Report of Dr. Katherine Keyes also reviews related studies.

Among respondents that began using opioids in the 1980s, the comparable figure was 30 percent.[45]

- Analysis of NSDUH survey data established that among respondents that reported using both heroin and prescription opioids (for non-medical use), the share that reported initially using prescription opioids was 83 percent in 2008-10.[46]

63. These studies and the analyses presented above in **Figures III.2** through **III.4** demonstrate that the increase in deaths due to illicit opioid use is closely related to the growth in demand for illicit drugs after 2010. Since the increased demand for illicit opioids would not have occurred absent defendants' misconduct resulting in increased shipments of prescription opioids and CSA registrants' failure to identify excessive shipments, the resulting harm relating to illicit opioids is appropriately attributable to defendants' actions. Simply stated, the available data indicate that in the absence of shipments of prescription opioids, the post-2010 increase in mortality due to heroin and fentanyl would not have occurred. This is also confirmed by the analysis below.

B. Statistical Models of the Impact of Prescription Opioid Shipments on Mortality

64. Statistical analysis of the impact of shipments of prescription opioids on mortality must recognize both the dramatic change in nature of the opioid crisis after 2010 discussed above, as well as the limitations of available data. This section motivates and outlines statistical

[45] Cicero, Theodore J., Matthew S. Ellis, Hilary L. Surratt, and Steven P. Kurtz. "The changing face of heroin use in the United States: A retrospective analysis of the past 50 years." *JAMA Psychiatry* 71 (2014): 821-826, p. 823.
[46] Jones, Christopher M. "Heroin use and heroin use risk behaviors among nonmedical users of prescription opioid pain relievers—United States, 2002–2004 and 2008–2010." *Drug and Alcohol Dependence* 132 (2013): 95-100, p. 97.

frameworks for estimating the impact of shipments of prescription opioids on opioid-related mortality that are informed by the changing nature of the crisis and other factors.

1. Framework 1: Direct Estimation of the Impact of Shipments of Prescription Opioids on Mortality

65. The "direct estimation" framework uses regression analysis to estimate the relationship between the increase in opioid-related mortality in a geographic area and per capita shipments of prescription opioids to that geographic area. The analysis yields estimates of the magnitude and statistical significance of that relationship. Regression analysis is a reliable and commonly used method to analyze the relationship between economic variables. It is widely used in the fields of economics and other social sciences and in expert analysis for the purposes of litigation.[47] Examples of regression analyses similar to the "direct estimation" approach are discussed further below.

a. Regression Specification

66. The regression framework used to estimate the relationship between opioid shipments to an area and changes in opioid-related mortality can be expressed as the following:

$$\begin{pmatrix} Change\ in\ opioid - \\ related\ mortality \end{pmatrix}_i = \beta_1 \begin{pmatrix} Opioid\ shipments \\ per\ capita \end{pmatrix}_i + X_i\beta + \varepsilon_i$$

The analysis evaluates the relationship between change in mortality between two periods of time (e.g. between 1995 and 2010) in a county (*i*) to per capita shipments to that county, as well as to various economic and demographic characteristics of the county (X_i). The

[47] See, for example: Daniel L. Rubinfeld, "Reference Manual on Multiple Regression," *Reference Manual on Scientific Evidence* 3rd. Ed. Federal Judicial Center, National Academies Press (2011): 303-358.

91. The estimated relationship between the growth in the opioid mortality rate and prescription opioid shipments to an area is shown in **Appendix III.H**. The first column shows the means of the dependent and independent variables. The average county had shipments equal to 1.45 MME per capita per day. The remaining columns show the coefficient estimates. Overall, the model fits well. The adjusted R^2 coefficient of 0.57 is quite high for cross-sectional regressions of changes in mortality rates.[73] The coefficients on the demographic and economic variables are generally as expected. Opioid-related mortality went up more in areas where people had fewer years of education and where economic conditions were worse.

92. The coefficient on opioid shipments is most important for this analysis. The coefficient is positive and significant statistically. The probability that a result of this magnitude would occur by chance is less than 1/100th of one percent. The results indicate that, all else equal, each unit increase in shipments between 1997 and 2010 (measured in MME per capita per day) raises the mortality rate by [redacted] deaths per 100,000, an increase of more than [redacted] percent over the average rate in the base period. A unit increase in shipments corresponds to a [redacted] percent increase from the [redacted] shipment level across all areas. In summary, these results show that even with very extensive controls for economic and social factors, there remains a strong, statistically significant, and large relationship between prescription opioid shipments and opioid-related mortality through 2010. The specific magnitude of this effect and its implication on the analysis is presented in the following section.

[73] The R^2 coefficient reflects the proportion of the variance in the dependent variable (here opioid-related mortality rates) that is explained by the variance in the independent variables (here prescription opioid shipments and demographic and economic variables). The adjusted-R^2 adjusts for the number of covariates included in the model, so that including more variables does not automatically indicate a better fit. This statistic can be used as a measure of the "goodness of fit" of the regression model.

2. Implementation of Indirect Model for Illicit Mortality Post-2010

93. As noted above, the indirect regression model estimates the relationship between the opioid mortality rate in an area and the economic and demographic characteristics of the area. The regression estimates are then used to project how opioid mortality would have changed in response to changes over time in the economic and demographic characteristics, but without misconduct on the part of the defendants.

94. The indirect regression model for the post-2010 period is used to evaluate how deaths due to illicit opioids would have changed after 2010 in response to changes in economic and demographic factors in the absence of the increased demand for illicit opioids. The regression model explains variation across counties in the average death rate due to use of illicit opioids in 2008-2010. The death rate due to use of illicit opioids is defined to include any death involving heroin and/or fentanyl.[74] The multiyear average is used to dampen any effect of random fluctuations in mortality due to use of illicit opioids. Like the direct regression, the indirect regression includes controls for county-specific demographic and economic characteristics. Demographic characteristics include: the distribution of area population by age, race, gender and educational attainment, as well as percent urban. Also included are economic indicators including the unemployment rate and employment-to-population ratio; median household income; the employment share by major industry sector; and the county's population. The independent variables are all measured based on the average from 2008-2010.

[74] As above, the data used in the indirect regression incorporate the adjustment proposed by Christopher Ruhm.

95. As in the direct analysis, the indirect regression model is estimated on data from large counties, as defined above and therefore, again, the data are not weighted in the model estimation. The regression model is estimated in "semi-log" form, in which mortality due to illicit opioids is expressed in logarithmic terms and other economic and demographic variables are not. This specification yields estimates of the (approximate) percentage effect on illicit mortality resulting from a unit change in economic and demographic factors.

96. **Appendix III.H** reports the variable means and coefficient estimates for this regression model. The overall model fits well, with an adjusted R^2 of 0.31. The regression results show many of the same features as with the direct model. As with the direct model, areas where the economy was worse by most measures have higher mortality.

97. The results of the regression model, together with data on explanatory variables for 2011-16 are then used to predict "but for" mortality rates for illicit opioids for 2011-16 that would have been observed in the absence of the shift into illicit opioids after 2010 that resulted from earlier shipments of prescription opioids. As shown in **Figure III.5**, deaths due to illicit opioid use increased dramatically after 2010 but projections of the average but for illicit mortality rate based on the 2008-10 regression indicate that illicit mortality would have fallen in the absence of the decline in shipments of prescription opioids and the increased demand for illicit opioids after that time. To understand this predicted decline, recall that, on average over the counties, the economy improved over this time period, so this component of the model predicts fewer opioid-related deaths.